Cutaneous Metastases from Visceral Carcinoma in Siriraj Hospital : A Retrospective Review

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Abstract : **Cutaneous metastases occurred in 0.1% of all patients with cancer. The most common primary tumor was carcinoma of the breast (47.8%). They were recognized after the primary tumor in 56.5%, and were the first sign of cancer in 30.5%, especially in carcinoma of the lung. However, they were not uncommon as an early indicator of metastatic disease. They tended to appear in areas overlying the primary carcinoma. Only carcinoma of lung and cervix may disseminate to distant cutaneous sites. The prognosis depended on the type of primary carcinoma. Carcinoma of the breast with cutaneous metastases had a prolonged survival. Survival of patients with carcinoma of the lung averaged 2 months after the appearance of cutaneous metastases.**

เรื่องย่อ : **มะเร็งแพร่กระจายสู่ผิวหนัง : การศึกษาย้อนหลังในโรงพยาบาลศิริราช**

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มะเร็งจากอวัยวะภายในแพร่กระจายสู่ผิวหนังพบได้ 0.1% ของผู้ป่วยมะเร็งทั้งหมด มะเร็งปฐมภูมิที่พบบ่อยที่สุดคือมะเร็งเต้านม (47.8%) มะเร็งแพร่กระจายสู่ผิวหนังส่วนใหญ่มักพบหลังการวินิจฉัยมะเร็งปฐมภูมิถึง 56.5% แต่ก็อาจพบมะเร็งแพร่กระจายสู่ผิวหนังก่อนการตรวจพบมะเร็งปฐมภูมิได้ 30.5% ซึ่งมักพบในมะเร็งปอด และพบมะเร็งแพร่กระจายสู่ผิวหนังก่อนที่จะแพร่กระจายไปสู่อวัยวะอื่นได้บ่อย ตำแหน่งที่พบมักอยู่ใกล้หรือบนตำแหน่งของมะเร็งปฐมภูมิ ยกเว้นมะเร็งปอดและมะเร็งปากมดลูก ที่พบได้ในบริเวณที่ห่างไกลออกไปได้ การพยากรณ์โรคหลังพบมะเร็งแพร่กระจายสู่ผิวหนังขึ้นกับชนิดของมะเร็งปฐมภูมิ มะเร็งเต้านมจะมีการพยากรณ์โรคดี แต่มะเร็งปอดมักเสียชีวิตภายใน 2 เดือนหลังพบมะเร็งแพร่กระจายสู่ผิวหนัง

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INTRODUCTION

Cutaneous metastases occur in 0.7% to 9% of all patients with cancer[1-6]. The evaluation of cutaneous metastases has profound diagnostic, therapeutic, and prognostic significance. They are often recognized after the primary tumor, and are uncommonly present at the time of diagnosis of cancer (1.3% of all patients with cancer), and even less commonly as the first sign of cancer (0.8% of all patients with cancer)[7]. Breast cancer is the most frequent source of cutaneous metastases. The most frequent primary tumor in men is carcinoma of the lung. Carcinoma of the breast is the most common primary tumor in women[8-10]. The discovery of cutaneous metastases in a patient with a known primary tumor may be the first indicator of recurrence. They are the first sign of extranodal disease in 7.6% of patients with metastatic carcinoma[11]. They have a poor prognosis, especially in patients with cancer of the lung, ovary, upper respiratory tract, or upper digestive tract[11-14] However, no data concerning cutaneous metastases in Thai patients is available. The purpose of this communication is to delineate the diagnostic, therapeutic, and prognostic significance of cutaneous metastases in Thai patients.

MATERIALS AND METHODS

The Tumor Registry at Siriraj Hospital from 1993-2000 was used to identify all patients with cancer and those with cutaneous metastases. Melanoma, squamous cell carcinoma , basal cell carcinoma, lymphoma, leukemia and sarcoma were excluded. The medical records were reviewed for additional information, including the location of skin metastases, the time of histopathological examination of the primary tumor and that of the cutaneous metastatic lesions and other metastatic organs, survival times of patients with skin metastases, and the histopathological findings.

RESULTS

The total number of patients with cancer from Tumor Registry data of Siriraj Hospital from 1993-2000 was 30,152 (Table 1). Cervical cancer was the most common tumor and breast cancer was the second. Cutaneous metastases were found in 23 of these patients, 9 men and 14 women (Table 2). The prevalence was 0.1%. Breast carcinoma was the most common primary tumor resulting in skin involvement and accounted for 11 (47.8%) of all patients with cutaneous metastases (Table 1). Among 14 women with cutaneous metastases, carcinoma of the breast was still the most common primary tumor in 64.4% (Table 2). In contrast, among 9 men with cutaneous metastases, the most common primary tumor was adenocarcinoma, with an unknown primary site in 33.4% (Table 2). Skin involvement occurred in 11(0.4%) of total breast cancer patients (Table 1). The frequency with which the cervical cancer metastasized to the skin was the lowest (0.02% of all cervical cancer patients). The most common histopathological finding was adenocarcinoma in 82.6% (Table 3). In patients presenting with cutaneous metastases of adenocarcinoma, carcinoma of lung and gastrointestinal tract were the most likely sites of the primary tumor after excluding carcinoma of the breast (Table 3).

Cutaneous metastases were recognized after the primary tumor in 13 patients (56.5% of all patients with cutaneous metastases). Breast cancer tended to spread to skin relatively late in the course of the disease, averaged 4 years 9 months after the diagnosis of the primary tumor. Ten patients (43.5% of all patients with cutaneous metastases) had cutaneous metastases at the time of presentation (Table 1). Cutaneous metastases developed at the same time as the diagnosis of primary tumor in 3 out of 10 (13% of all patients with cutaneous metastases), and 7 out of 10 (30.5% of all patients with cutaneous metastases) had cutaneous metastases before the diagnosis of the primary tumor. Patients with cutaneous metastases occurring before the diagnosis of primary tumor included 3 patients with lung cancer (average 3 months before the diagnosis of primary tumor), and 4 patients with an unknown primary site (Table 1). Fourteen patients also had other organ metastases. In 8 of these patients (57.1% of all patients who had both cutaneous metastases and other organ metastases), cutaneous metastases occurred at the same time as or before other organ involvement (Table 1).

Table 1. Skin metastases from visceral carcinoma found during the period of 1993-2000.

Primary tumor	No. of cases (%)					Average time from diagnosis of skin metastases to death (mo.)
	Total	With skin metastases	With skin metastases at the same time/ before the diagnosis of primary tumor	With skin metastases at the same time or before/after other organ metastases	With skin metastases who died	
Breast	2,864	11(0.4)	3/0	3/5	1	11
Lung	1,517	3(0.2)	0/3	-	2	2
Stomach	498	1(0.2)	-	0/1	-	-
Rectum	669	1(0.1)	-	-	-	-
Cholangio-carcinoma	325	1(0.3)	-	-	-	-
Bladder	971	1(0.1)	-	1/0	-	-
Cervix	4,695	1(0.02)	-	-	-	-
Unknown primary site						
Adenocarci-noma	865	3(0.3)	0/3	3/0	-	-
Undifferen-tiated cell	171	1(0.6)	0/1	1/0	1	1
Miscellaneous	17,577	-	-	-	-	-
Total	30,152	23(0.1)	3(13)/7(30.5)	8(57.1)/6(42.9)	4	3.5

Table 2. Origins of skin metastases.

Men		Women	
Primary site	**Cases with skin metastases (%)**	**Primary site**	**Cases with skin metastases (%)**
Unknown primary site, adenocarcinoma	3 (33.4)	Breast	9 (64.4)
Breast	2 (22.2)	Lung	2 (14.3)
Lung	1 (11.1)	Stomach	1 (7.1)
Rectum	1 (11.1)	Unknown primary site, undifferentiated cell	1 (7.1)
Bladder	1 (11.1)	Cervix	1 (7.1)
Cholangiocarcinoma	1 (11.1)	Total	14 (100%)
Total	9 (100%)		

Table 3. Histopathological classification of metastases.

Primary site	Adenocarcinoma	Undifferentiated	Miscellaneous
Breast	11	-	-
Lung	3	-	-
Stomach	1	-	-
Rectum	1	-	-
Cholangiocarcinoma	-	-	1
Bladder	-	-	1 (transitional)
Cervix	-	-	1 (adenosquamous)
Unknown primary site	3	1	-
Total	19 (82.6%)	1 (4.3%)	3 (13.1%)

Table 4. Sites of distant skin metastases.

Primary site	Scalp	Face	Neck	Upper extremities	Chest wall	Abdomen	Back	Pelvis	Lower extremities	Multiple sites
Breast	-	-	-	-	5	-	1	-	-	5
Lung	1	-	-	-	1	-	-	-	-	1
Stomach	-	-	-	-	-	1	-	-	-	-
Rectum	-	-	-	-	-	-	-	1	-	-
Cholangiocarcinoma	-	-	-	-	-	-	-	-	-	1
Bladder	-	-	-	-	-	-	-	1	-	-
Cervix	-	-	-	-	1	-	-	-	-	-
Unknown primary site										
- Adenocarcinoma	1	-	1	-	-	-	-	-	-	1
- Undifferentiated cell	-	-	-	-	-	-	-	-	-	1
Total	2	-	1	-	7	1	1	2	-	9

Fourteen patients (60.9% of all patients with cutaneous metastases) had cutaneous metastases that were limited to a single region of the body (Table 4). Multiple areas were involved in 9 patients (39.1% of all patients with cutaneous metastases), especially in breast cancer. The chest wall was an area of predilection for cutaneous metastases in 15 patients (65.2% of all patients with cutaneous metastases). The face and lower extremities were not involved. Cancer of the breast and lung often metastasized to the chest wall, whereas cancer of the stomach, rectum, cholangiocar-cinoma, and bladder most often metastasized to the abdomen or pelvis. Only one case of lung cancer, and one case of cervical cancer metastasized to skin sites at a distance from the primary tumor, i.e., scalp and chest wall, respectively. There were only three cases of breast cancer and one case of bladder cancer whose local cutaneous metastases occurred in the preexisting surgical scar.

The clinical finding was a nodule or plaque. An ulcer was seen in only one case of lung cancer on the scalp. Inflammatory skin metastases were seen in three cases of breast cancer.

The follow up period after the diagnosis of cutaneous metastases was on average 11.3 months. There were only 4 patients who died after the development of cutaneous metastases, two of which had lung cancer, one had breast cancer, and one had an undifferentiated cell cancer with an unknown primary site. The average time from diagnosis of skin metastases to death was 3.5 months (Table 1). Eleven patients were lost to follow up. These included 4 cases of breast cancer, 1 case of lung cancer, 1 case of cholangiocarcinoma, 1 case of bladder cancer, 3 cases of adenocarcinoma with unknown primary site, and 1 case of cervical cancer.

DISCUSSION

The frequency of cutaneous metastases was 0.1% of all patients with cancer, which was lower than the average frequency of 0.7 to 9% reported in the other studies[1-6]. This 0.1% frequency most likely underestimated the ultimate frequency of skin metastases in cancer patients because it was highly probable that some skin metastases went unnoticed. In addition, there might be a long time lag from diagnosis of the primary tumor to recognition of skin metastases. This study reaffirms previous observations that breast cancer is the most frequent source of cutaneous metastases[8-10]. This is true not only because breast cancer is common but also because it often involves the skin. The frequency of skin metastases from breast cancer was the second most common. Lookingbill[7] found that skin involvement occurred in 23.9% of breast cancer patients. In contrast, although cervical cancer is more common than breast cancer, the frequency with which this cancer metastasizes to the skin is the lowest. Lookingbill[7] found that only 0.3% of cervical cancer had cutaneous metastasis. The most common underlying tumor in women was breast cancer (64.4%), which corresponded to previous study (69%)[9]. In men, the most common primary tumor was adenocarcinoma of unknown primary site. In contrast, Brownstein[9] reported that lung cancer was the most common underlying tumor in men. Adenocarcinoma was the most common histopathological type in both men and women. In both men and women presenting with cutaneous metastases of adenocarcinoma, the lung and gastrointestinal tract were more likely to be the primary sites after excluding breast cancer, as in Brownstein's study[9]. Additional information from this study showed that when cutaneous metastasis of adenocarcinoma was the first sign, the primary site was likely to be lung. Gastrointestinal cancer tended to spread to skin following the diagnosis of the primary tumor.

Cutaneous metastases were recognized after the primary tumor in 56.5%. Breast cancer tended to spread to skin relatively late in the course of the disease. Skin involvement was uncommonly the first sign of cancer in 30.5%. Cutaneous metastases from lung cancer were recognized before the primary tumor in all three cases, on average 3 months before. Although cutaneous metastases uncommonly served as the first sign of cancer, they were not uncommon as early indicators of metastatic disease in 7.6% of all patients with metastatic disease[7,11]. The total number of patients with metastatic disease was not available in this study. However, this study showed that skin involvement occurred at the same time as or before other organ involvement in 57.1% of all patients who had both cutaneous metastases and other organ metastases.

Most patients (60.9%) had cutaneous metastases that were limited to a single region of the body, as in Brownstein's study[9]. Chest wall was the area of predilection for cutaneous metastasis, whereas face and lower extremities were not involved. This study was in agreement with a previous study[9] that the tumors spread to skin in definite patterns. Most cutaneous metastases, such as breast cancer, appeared in areas overlying or in the vicinity of the primary tumor, usually following the primary tumor, and spread to the skin largely through lymphatic channels[8,9]. On the other hand, cutaneous metastatic lesions from tumors, such as carcinoma of the lung and cervix, appeared at a distance from the primary tumor. Cancers that tend to invade veins, such as lung cancer, often present as cutaneous metastasis in skin sites distant from the primary tumor, and often precede recognition of the underlying tumor[8,9]. In a series of 15 patients, the most common sites of cutaneous metastases from carcinoma of the cervix were abdominal wall and vulva, followed by anterior chest wall[15], as in this study. Also as in previous study,[16] cutaneous metastases from carcinoma of the cervix was unusual as the first sign of disease. As has previously been described, local metastases may develop in scars at the surgical incisional site for the primary tumor, usually appearing within a year of surgery[10]. However, they may also be present in unrelated surgical or traumatic scar sites. They may be the first sign of breast, ovarian, colorectal, liver, oral, laryngeal, lung, renal and endometrial cancers. Thus new nodules in old scars should be examined histologically, as should nodules in new scars. In this study, surgical scar metastases were found in three patients with breast cancer and one case of bladder cancer in the excisional scar for the primary tumor.

The clinical finding was a nodule or plaque. An ulcer was seen in only one case of lung cancer on the scalp. Inflammatory skin metastases were seen in three cases of breast cancer. They have been well described in breast cancer[10], but have also been rarely reported in other types of cancer, including pancreatic[17], rectal[18], lung[19], ovarian[20], parotid cancers[21], and melanoma[22]. However, they are uncommon.

Reingold[4] reported that his patients survived an average of only 3 months after the development of cutaneous metastases. The patients in this study fared better, probably because of advances in cancer therapy during the past few decades. Nevertheless, cutaneous metastases still have a poor prognosis, especially in patients with cancer of the lung, ovary, upper respiratory tract, or upper digestive tract[11]. This study showed that the prognosis depended on the type of primary carcinoma. Breast cancer with cutaneous metastases had a prolonged survival. Survival of patients with lung cancer averaged 2 months after the appearance of cutaneous metastases.

REFERENCES

1. Gates O. Cutaneous metastases of malignant disease. Am J Cancer 1937; **30:** 718-730.
2. Abrams HL, Siro R, Goldstein N. Metastases in carcinoma: analysis of 1,000 autopsied cases. Cancer 1950; **3:** 74-85.
3. Enticknap JB. An analysis of 1,000 cases of cancer with special reference to metastasis. Guy's Hosp Rep 1952; **101:** 273-279.
4. Reingold IM. Cutaneous metastases from internal carcinoma. Cancer 1966; **19:** 162-168.
5. McWhorter JE, Cloud AW. Malignant tumors and their metastases: a summary of the necropsies on eight hundred sixty-five cases performed at the Bellevue Hospital of New York. Ann Surg 1930; **92:** 434-443.
6. Spencer PS, Helm TN. Skin metastases in cancer patients. Cutis 1987; **39:** 119-121.
7. Lookingbill DP, Spangler N, Sexton FM. Skin involvement as the presenting sign of internal carcinoma: a retrospective study of 7,316 cancer patients. J Am Acad Dermatol 1990; **22:** 19-26.
8. Brownstein MH, Helwig EB. Metastatic tumors of the skin. Cancer 1972; **29:** 1298-1307.
9. Brownstein MH, Helwig EB. Patterns of cutaneous metastasis. Arch Dermatol 1972; **105:** 862-868.
10. Brownstein MH, Helwig EB. Spread of tumors to the skin. Arch Dermatol 1973; **107:** 80-86.
11. Lookingbill DP, Spangler N, Helm KF. Cutaneous metastases in patients with metastatic carcinoma: a retrospective study of 4,020 patients. J Am Acad Dermatol 1993; **29:** 228-236.
12. Terashima T, Kanazawa M. Lung cancer with skin metastasis. Chest 1994; **106:** 1448-1450.

13. Lucas FV, Perez-Mesa C. Inflammatory carcinoma of the breast. Cancer 1978; **41:** 1595-1605.
14. Bozztti F, Saccozzi R, De Lena M, et al. Inflammatory cancer of the breast: analysis of 114 cases. J Surg Oncol 1981; **18:** 355-361.
15. Imachi M, Tsukamoto N, Kinoshita S, et al. Skin metastasis from carcinoma of the uterine cervix. Gynecol Oncol 1993; **48:** 349-354.
16. Schwartz RA. Cutaneous metastatic disease. J Am Acad Dermatol 1995; **33:** 161-182.
17. Edelstein JM. Pancreatic carcinoma with unusual metastasis to the skin and subcutaneous tissue simulating cellulitis. N Engl J Med 1950; **242:** 779-781.
18. Reuter MJ, Nomland R. Inflammatory cutaneous metastatic carcinoma. Wis Med J 1941; **40:** 196-201.
19. Ingram JT. Carcinoma erysipelatodes and carcinoma telangiectaticum. Arch Dermatol 1958; **77:** 227-231.
20. Krishnan EU, Phillips AK, Randell A, et al. Bilateral metastatic inflammatory carcinoma in the breast from primary ovarian cancer. Obstet Gynecol 1980; **55 (Suppl):** 94-96.
21. Schwartz RA, Rubenstein DJ, Raventos A, et al. Inflammatory metastatic carcinoma of the parotid. Arch Dermatol 1984; **120:** 796-797.
22. Haupt HM, Hood AF, Cohen MH. Inflammatory melanoma. J Am Acad Dermatol 1984; **10:** 52-55.